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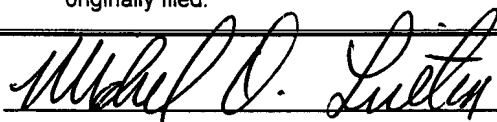
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US00523065A

United States Patent [19]

Cook et al.

[11] Patent Number: 5,623,065

[45] Date of Patent: Apr. 22, 1997

[54] **GAPPED 2' MODIFIED OLIGONUCLEOTIDES**[75] Inventors: **Phillip D. Cook, Vista; Brett P. Monia, Carlsbad, both of Calif.**[73] Assignee: **Isis Pharmaceuticals, Inc., Carlsbad, Calif.**[21] Appl. No.: **244,993**[22] PCT Filed: **Dec. 23, 1992**[86] PCT No.: **PCT/US92/11339**§ 371 Date: **Jun. 21, 1994**§ 102(e) Date: **Jun. 21, 1994**[87] PCT Pub. No.: **WO93/11339**PCT Pub. Date: **Jul. 8, 1993****Related U.S. Application Data**

[63] Continuation-in-part of Ser. No. 814,961, Dec. 24, 1991, abandoned, and Ser. No. 566,977, Aug. 13, 1990, abandoned.

[51] Int. Cl.⁶ **C07H 21/00; C07H 21/02; C07H 21/04**[52] U.S. Cl. **536/23.1; 536/23.2; 536/23.5; 536/23.51; 536/23.52; 536/23.53; 536/25.1; 536/25.2; 435/91.1; 435/91.2; 435/91.5; 935/6; 935/9; 935/10**[58] Field of Search **514/44; 536/23.1; 536/23.2, 23.5, 23.51, 23.52, 23.53, 25.1, 25.2; 435/91.1, 91.2, 91.4, 91.5; 935/9, 6, 10**[56] **References Cited****U.S. PATENT DOCUMENTS**

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Primary Examiner—Christopher S. F. Low**Attorney, Agent, or Firm**—Woodcock Washburn Kurtz Mackiewicz & Norris[57] **ABSTRACT**

Oligonucleotides and other macromolecules are provided that have increased nuclease resistance, substituent groups for increasing binding affinity to complementary strand, and subsequences of 2'-deoxy-erythro-pentofuranosyl nucleotides that activate RNase H enzyme. Such oligonucleotides and macromolecules are useful for diagnostics and other research purposes, for modulating protein in organisms, and for the diagnosis, detection and treatment of other conditions susceptible to antisense therapeutics.

19 Claims, 2 Drawing Sheets

D-10-61